

Retro-1,4-cycloaddition of Adducts Derived from Steroidal-5,7-dienes and 4-Phenyl-1,2,4-triazoline-3,5-dione

By MASAO TADA* and ATSUSHI OIKAWA

(*The Research Institute for Tuberculosis and Cancer, Tohoku University, Seiryomachi 4-1, Sendai 980, Japan*)

Summary Heating at 120 °C of 1,4-cycloadducts of various steroidal-5,7-dienes and 4-phenyl-1,2,4-triazoline-3,5-dione with mineral base in an appropriate solvent gives the corresponding steroidal-5,7-dienes in high yields.

CONJUGATED dienes may be protected by reaction with a dienophile; 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) undergoes cycloaddition to steroidal-5,7-dienes providing 1,4-cycloadducts.^{1,2} Barton *et al.*² reported that the diene system could be regenerated in high yield by treatment of these adducts with lithium aluminium hydride. As part of our investigation of reversible protection of steroidal-5,7-diene systems, we report here a simple method for the retro-1,4-cycloaddition of adducts derived from steroidal-5,7-dienes and PTAD.

The adduct (**1b**)² (1 mmol) and anhydrous K₂CO₃ (1 mmol) in dimethyl sulphoxide† were heated at 120 °C for 7 h with stirring to give ergosteryl acetate (**2b**) in quantitative yield. An analogous result was obtained with the ergosterol adduct (**1a**).^{1,2} The retro-1,4-cycloaddition of (**1c**), m.p. 154–155 °C, obtained from either (**1a**) or (**2c**),³ in the presence of anhydrous K₂CO₃ in Me₂SO also afforded (**2c**) in quantitative yield. When pyridine was used in place of K₂CO₃, the retro-addition of adducts (**1**) proceeded so slowly that 90% of (**1**) was recovered. In the conversion of (**1**) into (**2**), Me₂SO and *NN*-dimethylformamide were better solvents than ethylene glycol or methyl cellosolve. Yields were optimum at 120 °C and for 7 h reaction. Cleavage of (**1b**) using an aqueous solvent system was accompanied by removal of the acetyl group of (**1b**) to furnish ergosterol (**2a**)

† All solvents were dried with molecular sieves and all new compounds gave correct analyses and spectral data.

in 88% yield. Adduct (3) (m.p. 142—144 °C; 74%) derived from the ether (4c) was converted into (4c) in 95% yield under similar conditions. Treatment of (4c) with dilute

HCl in ethanol gave the diol (4a) in high yield. Crump *et al.* reported that the reduction of (5b) with LiAlH_4 gave the 22-hydroxy derivative (4a), the position of the hydroxy group being confirmed by mass spectroscopy.⁴ Treatment of (5c) with LiAlH_4 in an analogous fashion gave a 3:1 mixture of the 22-hydroxy compound (4c), m.p. 169—170 °C, and the 23-hydroxy compound, m.p. 133—134 °C, the locations of the hydroxy groups being established by mass spectral analysis of their trimethylsilyl derivatives, prepared with *N,O*-bis(trimethylsilyl)acetamide in pyridine. Treatment of (4c) with acetic anhydride and *p*-chlorobenzoyl chloride in pyridine afforded the acetate, m.p. 163—164 °C, and the *p*-chlorobenzoate, m.p. 201—202 °C, respectively.

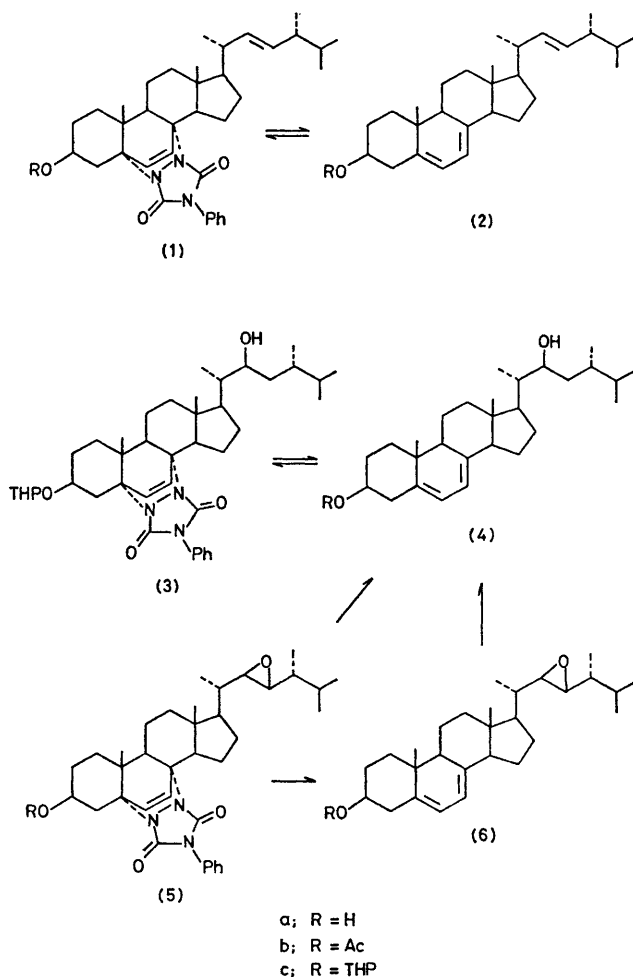
Treatment of the adduct (5b),⁴ derived from (1b), under similar conditions resulted in retro-cycloaddition without affecting the epoxide ring to give 22,23-epoxyergosteryl acetate (6b), m.p. 133—134 °C, in 83% overall yield from (1b). The adduct (5c) was prepared by epoxidation of (1c) with *m*-chloroperbenzoic acid in CH_2Cl_2 . The analogous conversion of (5c) gave 22,23-epoxyergosteryl tetrahydropyranyl ether (6c), m.p. 138—139 °C, in 91% yield based on (1c). Hydrolysis of (6c) with HCl in ethanol furnished 22,23-epoxyergosterol (6a), m.p. 138—139 °C, in 94% yield. Compound (6a) was also obtained in 95% yield by heating (6b) for 10 min with 2*N* KOH in refluxing aqueous methanol. Reduction of (6c) with LiAlH_4 gave both (4a) and the 23-hydroxy derivative in a ratio of 1:4, in contrast to the reduction of the adduct (5c).

Treatment of the 1,4-cycloadduct (m.p. 156—157 °C) of 7-dehydrocholesterol and PTAD in an analogous fashion gave a 52% yield of 7-dehydrocholesterol.

This method is useful because of its simplicity and the high yields obtained as well as its applicability to compounds having groups which are sensitive to LiAlH_4 .

We thank Dr. Kyoza Ogura, Tohoku University, for the mass spectral determinations and helpful discussions.

(Received, 2nd May 1978; Com. 470.)



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